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Research Note

Sensory Experiences in Man Evoked by Intraneural Electrical Stimulation of Intact Cutaneous Afferent Fibers*

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Summary. The response of slowly conducting myelinated and unmyelinated afferent units to natural types of cutaneous stimuli was recorded extracellularly with tungsten microelectrodes from intact human skin nerves. Seven fibers had characteristics of C-polymodal units (conduction velocity: 0.75–1.2 m/s) and two fit descriptions of myelinated high-threshold mechanoreceptors (conduction velocity of one: 19 m/s).

Attempts were made to evoke a sensation in a subject by stimulating the impaled fascicles directly with electrical pulses of controlled amplitude, duration and frequency so as to try to correlate responsive properties of the sensory units and sensory experience. The subjective sensations evoked by natural stimuli to the skin surface were used as criteria for comparison.

Key words: Human sensory nerve – C-polymodal nociceptors – High-threshold mechanoreceptors – Electrical stimulation – Sensation

The hypothesis that the responsive properties of primary sensory units can serve as valid criteria for modalities of sensation has long been the subject of controversy (von Frey 1869; Ranson and Billingsley 1916; Adrian et al. 1931; Heinbecker et al. 1933; Sinclair 1955; Collins et al. 1960; Dyck et al. 1971; Mackenzie et al. 1975). We approached this question in the present study by combining Vallbo and Hagbarth's (1967) technique of microneurography for recording unitary impulses in nerves of man with an attempt to initiate discharges directly in intact single afferent fibers by electrical stimulation through the recording microelectrode. The purpose was to correlate the peripheral nerve signals evoked by natural stimuli with the subjective sensory experience that their stimulation elicited in conscious human subjects. In the present study, unitary discharges deriving from large diameter myelinated A–fibers that were recorded from in all experimental sessions were not considered. Our particular interest lay in whether activation of specifically slowly conducting myelinated fibers and/or unmyelinated (C) fibers of sensory elements with nociceptive characteristics (Bessou and Perl 1969; Burgess and Perl 1967; Perl 1968) causes painful sensations in man since it is well established that excitation of slowly conducting afferent fibers evokes pain and that nociceptive primary afferent units exist in man (Landau and Bishop 1953; Collins et al. 1960; Van Hees and Gybels 1972; Hallin and Torebjörk 1973; Torebjörk and Hallin 1973; Burke et al. 1975; Willer 1977). Such data could contribute further toward the understanding of the degree to which sensory modalities are mediated by different peripheral afferent fibers.

Methods

The observations were made on 4 awake volunteers (one female and three males) from the laboratory staff. All experiments were done on the superficial branch of the left radial nerve. Unitary potentials were recorded with Hostaflon TF coated tungsten microelectrodes (Konietzny and Hensel 1974). The left arm of a relaxed subject sitting in a dental chair was abducted and the forearm, radial side up, was embedded in a vacuum cast for immobilization. The sensory nerve to be explored was located by palpation and the recording microelectrode was inserted through the sterilized skin into the nerve about 2 cm proximal to the wrist. The indifferent electrode consisted of a saline-soaked gauze pad on the subject's arm. Signals from the recording electrode were amplified by a high input impedance differential AC amplifier,

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Table 1. Cutaneous receptors in the human subject with myelinated and unmyelinated afferent fibers in the superficial radial nerve. Responsiveness to the indicated stimulus quality is shown by number of +

Unit no.	von Frey Threshold (g)	Conduction-Velocity (m/s)	Receptive Field	Pressure	Forceps Needle	Noxious Heat	Cooling	Remarks
(1) High-threshold mechanoreceptor					+	–	–	Highly regular slowly adapting discharge
(2) Polymodal Nociceptor	2			++	++	+	–	
(3) Polymodal Nociceptor	2	0.82	Area 1 cm^2 with overlapping receptive fields containing two discrete spots	–	++	+	–	
(4) Polymodal Nociceptor	3	0.75		–	++	+	–	
(5) Polymodal Nociceptor	2.4	0.88	Elliptical Area 10 mm long	+	+++	++	–	After discharge
(6) Polymodal Nociceptor		0.83	Area 12 × 8 mm					
(7) Polymodal Nociceptor		1.2				+		
(8) Polymodal Nociceptor		1.07				+		
(9) High-threshold mechanoreceptor	0.4	19	Area 7 × 5 mm with 12 active spots	+	++	–	–	
(10) High-threshold mechanoreceptor?		20						

displayed on an oscilloscope and reproduced by an auditory monitor. While recording, the microelectrode was manually manipulated by small displacements within the nerve in attempt to isolate activity of appropriate single fibers. A variety of forms of cutaneous stimulation was systematically used in order to test the biophysical specificity of the units (Hensel 1974). Once a single fiber was isolated, testing always began with gentle mechanical stimulation such as brushing, lighth contact with a smoothly rounded glass rod and probing the skin with graduated von Frey hairs. The latter were used to obtain force threshold data and to map the receptive field. Then, stronger stimuli were used (stiff von Frey stimulators, sharp probes – a sharpened point of a wooden stick or a steel needle, pinching the skin by a pair of forceps). Innocuous warming and noxious heat were produced by radiant heat. Cooling was produced by ether or ethyl chloride evaporation from the skin. Skin surface temperature was estimated by a contact thermistor. Regions yielding responses were marked by felt-tip pencil. The recording microelectrode could be switched to an isolated stimulator with a high impedance output for passage of constant-current electrical pulses to stimulate axons near the electrode tip. Conduction velocities of afferent fibers were calculated from latency of potentials evoked by electrical stimulation of the receptive field by single short duration pulses and the distance between the stimulating and recording electrode.

Subjects were asked to report and to describe the sensations evoked by the various natural stimuli and those elicited by the electrical intraneural stimuli in terms familiar to them.

Results

Unitary discharges were recorded from nine afferent fibers identified by their response to natural stimulation. Of these, seven were classified as C-fiber, polymodal nociceptors according to the characteristics described by Bessou and Perl (1969). Two other fibers had the responsive characteristics of another type of nociceptive element, the high-threshold mechanoreceptors with myelinated fibers (Burgess and Perl 1967; Perl 1968). Table 1 summarizes some characteristics of the sample. The receptive fields of the units considered to be polymodal nociceptors were roughly circular or elliptic areas of approximately 1 cm^2. The most effective stimuli for their excitation were noxious manipulation of the receptive field, e.g. squeezing with a pair of forceps or a needle penetrating the skin. They did not respond to gentle mechanical stimultion of the skin or to cooling. Most of this group were tested for and responded to noxious heat at skin temperatures of about 50° C (temperatures over 55° C were not used to limit damage to the skin). Conduction velocities determined for six units varied from 0.75 to 1.2 m/s, consistent with the supposition that these kinds of units are predominantly innervated by C-fibers. Polymodal nociceptors of a similar type have been previously described in monkey (Kumazawa and Perl 1977) and in cat (Bessou and Perl 1969; Beck et al. 1974) and in human skin nerves (Van Hees and Gybels 1972; Hallin and Torebjörk 1974; Torebjörk and Hallin 1974; Konietzny and Hensel 1979).

Neither of the high-threshold mechanoreceptors could be excited by moderate intensity moving or static displacements of the skin; however, intense mechanical stimulation produced by sharp objects pressed against the skin consistently elicited a burst of discharges. The conduction velocity for one high-threshold mechanoreceptor was determined to be 19 m/s, putting it into the Aδ group. Contribution velocity determination were not made for the other unit definitely be classified as of the same type by its responses to natural stimuli. The functional study of the third similar unit with a conduction velocity of 20 m/s was incomplete and it is marked with a "?" in Table 1. None of the units considered probable high-threshold mechanoreceptors responded to cold or heat stimuli. The latter and the consistent evocation of activity by strong mechanical stimuli fit characteristics of the high-threshold mechanoreceptors described in the cat (Bessou and Perl 1969; Burgess and Perl 1967) and monkey (Perl 1968).

Electrical stimulation through the microelectrode evoked sensations at moderate current intensity only when good unitary recordings were present. The following describes our observations in which clear reports of sensory experiences were encountered.

1) At threshold of 20 μA for 50 μs pulses at 3–4 Hz the subject J.S. (♂) reported a sensation to be a prick, similar to that produced by a pointed wooden stick; it was referred to a skin area on the dorsal surface of the hand between second and third metacarpal. When the stimulation frequency was reduced to 0.5 Hz a feeling of pricking pain was reported in the same region. When the stimulation frequency was raised again to 3–4 Hz the resulting sensation was described as burning. After these tests with the microelectrode in the recording mode, two different polymodal nociceptive units (units nos. 3 and 4) were found to respond to a pointed probe pressed against the region of the skin described as the region of the sensation elicited by electrical pulses.

2) The sensation reported by subject V.M. (♀) for pulses of 50 μs duration at 10 μA and a repetition frequency of 0.5 Hz was a vague fuzzy feeling on the skin over the tendon of the third finger, 2 cm proximal to the first phalangeal joint. When ordinarily painful mechanical stimuli were applied to the field of the skin that corresponded to the referral area for the electrical stimulus, a polymodal nociceptive unit (unit no. 6) was activated. Subsequently, the stimulus current was increased and at 28 μA the subject reported a definite tap, such as would lightly indenting the skin between more distally and 3rd phalangeal joint of the 3rd finger. Increasing the stimulus strength further to 40 μA continued to evoke the tap feeling but with repetition this sensation faded as the electrical stimulation continued. From the region of this latter referral a small amplitude multiunit A-fiber response was evoked by gentle mechanical stimuli. At a stimulus current of 100 μA the subject reported the sensation now was a weak prick back in the receptive field of unit no. 6. At a stimulus current of 120 μA the feeling of prick became more intense and was equated to a needle penetrating the skin at the same locus.

3) Repositioning of the microelectrode in subject V.M. located a high-threshold mechanoreceptive unit (unit no. 9). Electrical stimulation with 50 μs pulses at 0.5 Hz through the microelectrode evoked a paraesthetic (unpleasant) "tap" sensation on the skin about 1 cm proximal to the receptive field of the units described in 2) above. Mechanical stimuli applied to this proximal skin field activated a slowly adapting, high-threshold mechanoreceptor. (It could not be determined whether or not this unit was the one previously identified as no. 9.) Increasing the intensity of the electrical stimulus to 80 μA evoked a sensation of pricking pain that was referred to skin 3–4 cm still further proximal than the receptive field of the high-threshold mechanoreceptor. Natural stimulation of the new field of referral uncovered two units identified as of the polymodal nociceptive type (units nos. 7 and 8). Intradermal electrical stimuli at the latter skin field elicited the response of a slowly conducting (Aδ) unit with a conduction velocity of 20 m/s. It was not possible to evoke discharges from this last element by natural stimuli, presumably because its threshold was above that intensity we wished to use. The experiments do not exclude completely the influence of the intraneural electrical stimulation on the excitation of other groups of afferent fibers though they have not been recorded from at the same experimental situation. Due to its low electrical threshold the large diameter myelinated A-fiber group might have been simultaneously activated by the electrical stimuli. However, Hagbarth et al. (1970) have emphasized that depending on the arrangement of individual nerve fibers in small fascicles surrounded by perineural sheats of collagen lamellae "overhearing" between neighbouring fascicles is negligible.

Single unit recordings have been obtained with little or no interference from activity in surrounding axons both from large myelinated fibers with small or often spot-like receptive fields with sharp boundaries on the skin (Hagbarth et al. 1970) and even from small myelinated (Aδ) or unmyelinated (C) fibers (Croze et al. 1976; Konietzny and Hensel 1979).

Accordingly, our investigations indicate that a sharp localization of a natural stimulus and the sensation evoked in the same receptive field on the skin was obtained upon direct electrical stimulation of the impaled nerve fascicles.

These and other observations indicate that sensory nerve fibers seem to be grouped together in certain small nerve bundles well isolated from adjacent axons.

As mentioned by Hallin and Torebjörk (1973) the arrangement of nerve fibers in small fascicles surrounded by perineural sheats of high impedance (Rashbass and Rushton 1949) might fascilitate the recording of single fiber activity from both myelinated and unmyelinated nerve fibers.

On the other hand, it seems likely that electrical stimuli delivered directly to the impaled nerve fascicles might be restricted in certain cases to those fibers where single afferent activity has been recorded from previously.

In conclusion, our results are consistent with the assumption that a functional specificity of the sensory terminals of peripheral nerve fibers underlies different cutaneous modalities. We found it most significant that the microelectrode was recording from high threshold cutaneous receptors whenever reasonable intensities of intraneural electrical stimuli evoked sensation reported as painful. In particular our observations suggest (a) that unmyelinated (C) polymodal nociceptive fibers are involved in perceptual events experienced as painful and (b) that particular relatively slowly conducting myelinated fibers in human skin nerves are related to the sensation caused by strong cutaneous mechanical stimulation, also reported as disagreable or painful.

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